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=> d his ful

     (FILE 'HOME' ENTERED AT 10:00:33 ON 12 JAN 2006)

     FILE 'HCAPLUS' ENTERED AT 10:01:04 ON 12 JAN 2006
               E ANTIBODIES/CT
               E E3+ALL
               E E2+ALL
L1          498 SEA ABB=ON  PLU=ON  ANTIBODIES AND IMMUNOGLOBULINS+PFT,NT/CT(L)
               CATALYTIC
L2         2157 SEA ABB=ON  PLU=ON  L1 OR CATALYT?(5A)ANTIBOD?
               E LIGAND/CT
               E E3+ALL
               E E2+ALL
L3         3463 SEA ABB=ON  PLU=ON  LIGANDS+PFT,NT/CT(L)RECEP?
L4        52088 SEA ABB=ON  PLU=ON  LIGAND(5A)RECEP? OR L3
L5           10 SEA ABB=ON  PLU=ON  L2 AND L4
L6        32512 SEA ABB=ON  PLU=ON  ?IMMUNOGEN?
L7            2 SEA ABB=ON  PLU=ON  L5 AND L6
L8        82596 SEA ABB=ON  PLU=ON  TUMO?(3A)NECROS?(3A)FACT? OR TNF
L9            3 SEA ABB=ON  PLU=ON  L5 AND L8
L10          10 SEA ABB=ON  PLU=ON  L5 OR L7 OR L9
L11       90486 SEA ABB=ON  PLU=ON  LIGAND(P)RECEP? OR L3
L12       90486 SEA ABB=ON  PLU=ON  L11 OR L3
L13          17 SEA ABB=ON  PLU=ON  L12 AND L2
L14           6 SEA ABB=ON  PLU=ON  L13 AND (L8 OR L6)
L15          17 SEA ABB=ON  PLU=ON  L13 OR L14 OR L10

     FILE 'MEDLINE, EMBASE, BIOSIS, USPATFULL, USPAT2, WPIX' ENTERED AT
     10:06:46 ON 12 JAN 2006
L16       12795 SEA ABB=ON  PLU=ON  (ANTIBOD? OR IMMUNOGLOBUL?)(S) CATALYT?
L17       21593 SEA ABB=ON  PLU=ON  (ANTIBOD? OR IMMUNOGLOBUL?)(P) CATALYT?
L18      173466 SEA ABB=ON  PLU=ON  IMMUNOGEN? OR NONIMMUNOGEN?
L19        4432 SEA ABB=ON  PLU=ON  L17 AND L18
L20        4269 SEA ABB=ON  PLU=ON  L16 AND L18
L21        4432 SEA ABB=ON  PLU=ON  L19 OR L20
L22      279141 SEA ABB=ON  PLU=ON  LIGAND(P) RECEPTOR
L23      317522 SEA ABB=ON  PLU=ON  TUMO?(3A) NECROS?(3A) FACT? OR TNF
L24        2644 SEA ABB=ON  PLU=ON  L21 AND L22
L25        1562 SEA ABB=ON  PLU=ON  L23 AND L24
L26      241306 SEA ABB=ON  PLU=ON  (TUMO?(3A) NECROS?(3A) FACT? OR TNF)(3A)(AL
               PHA OR A)
L27        1231 SEA ABB=ON  PLU=ON  L25 AND L26
               D KWIC
L28         153 SEA ABB=ON  PLU=ON  L27 AND CATALYT?(3A)(ANTIBOD? OR IMMUNOGLOB
               ?)
               D KWIC
L29        9580 SEA ABB=ON  PLU=ON  NONIMMUNOGEN? OR NON IMMUNOGEN?
L30          55 SEA ABB=ON  PLU=ON  L28 AND L29
               D KWIC
L31         142 DUP REM L28 (11 DUPLICATES REMOVED)
                    ANSWERS '1-141' FROM FILE USPATFULL
                    ANSWER '142' FROM FILE WPIX

     FILE 'HCAPLUS, USPATFULL, USPAT2, WPIX' ENTERED AT 10:14:38 ON 12 JAN 2006
L32          69 DUP REM L15 L30 (3 DUPLICATES REMOVED)
                    ANSWERS '1-17' FROM FILE HCAPLUS
                    ANSWERS '18-68' FROM FILE USPATFULL
                    ANSWER '69' FROM FILE WPIX
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             D L32 IBIB ABS HITIND 1-69
L33        129 SEA ABB=ON  PLU=ON  L28 AND MODULAT?
L34          5 SEA ABB=ON  PLU=ON  L33 AND PY<2002
L35         75 SEA ABB=ON  PLU=ON  L27 AND PY<2002
L36         62 SEA ABB=ON  PLU=ON  L35 AND MODULAT?
             D KWIC 10
             D QUE
L37       7603 SEA ABB=ON  PLU=ON  NONIMMUNOGEN? OR NON IMMUNOGEN? OR
             "NOT"(W) IMMUNOGEN?
L38        438 SEA ABB=ON  PLU=ON  L17 AND L37
L39        160 SEA ABB=ON  PLU=ON  L38 AND L26
L40        152 SEA ABB=ON  PLU=ON  L39 AND MODULAT?
L41          5 SEA ABB=ON  PLU=ON  L40 AND PY<2002
             D SCA
```

FILE HOME

FILE HCAPLUS

FILE COVERS 1907 - 12 Jan 2006 VOL 144 ISS 3
FILE LAST UPDATED: 11 Jan 2006 (20060111/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE MEDLINE
FILE LAST UPDATED: 11 JAN 2006 (20060111/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 will soon be available. For details on the 2005 reload, enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate

FILE EMBASE
FILE COVERS 1974 TO 6 Jan 2006 (20060106/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 11 January 2006 (20060111/ED)

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 10 Jan 2006 (20060110/PD)
FILE LAST UPDATED: 10 Jan 2006 (20060110/ED)
HIGHEST GRANTED PATENT NUMBER: US6986161
HIGHEST APPLICATION PUBLICATION NUMBER: US2006005290
CA INDEXING IS CURRENT THROUGH 10 Jan 2006 (20060110/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 10 Jan 2006 (20060110/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Oct 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2005

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<

>>> USPATFULL and USPAT2 can be accessed and searched together <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE USPAT2

FILE COVERS 2001 TO PUBLICATION DATE: 10 Jan 2006 (20060110/PD)
FILE LAST UPDATED: 10 Jan 2006 (20060110/ED)
HIGHEST GRANTED PATENT NUMBER: US2005272520
HIGHEST APPLICATION PUBLICATION NUMBER: US2006004269
CA INDEXING IS CURRENT THROUGH 10 Jan 2006 (20060110/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 10 Jan 2006 (20060110/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Oct 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2005

USPAT2 is a companion file to USPATFULL. USPAT2 contains full text of the latest US publications, starting in 2001, for the inventions covered in USPATFULL. USPATFULL contains full text of the original published US patents from 1971 to date and the original applications from 2001. In addition, a USPATFULL record for an invention contains a complete list of publications that may be searched in standard search fields, e.g., /PN, /PK, etc.

USPATFULL and USPAT2 can be accessed and searched together through the new cluster USPATALL. Type FILE USPATALL to enter this cluster.

Use USPATALL when searching terms such as patent assignees, classifications, or claims, that may potentially change from the earliest to the latest publication.

FILE WPIX
FILE LAST UPDATED: 6 JAN 2006 <20060106/UP>
MOST RECENT DERWENT UPDATE: 200602 <200602/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER GUIDES, PLEASE VISIT:
http://scientific.thomson.com/support/products/dwpi/

>>> FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX FIRST VIEW - FILE WPIFV.
FOR FURTHER DETAILS:
http://scientific.thomson.com/support/products/dwpifv/

>>> THE CPI AND EPI MANUAL CODES WILL BE REVISED FROM UPDATE 200601.
PLEASE CHECK:
http://scientific.thomson.com/support/patents/dwpiref/reftools/classificat

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html <

=> dup rem l15 l41
PROCESSING COMPLETED FOR L15
PROCESSING COMPLETED FOR L41
L42 22 DUP REM L15 L41 (0 DUPLICATES REMOVED)
ANSWERS '1-17' FROM FILE HCAPLUS
ANSWERS '18-22' FROM FILE USPATFULL

=> d l42 ibib abs hitind 1-17

L42 ANSWER 1 OF 22 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:988866 HCAPLUS
DOCUMENT NUMBER: 143:318201
TITLE: Protein toxins: intracellular trafficking for targeted

therapy
AUTHOR(S): Johannes, L.; Decaudin, D.
CORPORATE SOURCE: Laboratoire 'Trafic et Signalisation', Institut Curie, UMR144 Curie/CNRS, Paris, Fr.
SOURCE: Gene Therapy (2005), 12(18), 1360-1368
CODEN: GETHEC; ISSN: 0969-7128
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The immunotoxin approach is based on the use of tumor-targeting **ligands** or **antibodies** that are linked to the **catalytic** (toxic) moieties of bacterial or plant protein toxins. In this review, we first discuss the current state of clin. development of immunotoxin approaches describing the results obtained with the two toxins most frequently used: diphtheria and Pseudomonas toxin-derived proteins. In the second part of the review, a novel concept will be presented in which the roles are inverted: nontoxic **receptor**-binding toxin moieties are used for the targeting of therapeutic and diagnostic compds. to cancer or immune cells. The cell biol. basis of these novel types of toxin-based therapeutics will be discussed, and we will summarize ongoing preclin. and clin. testing.
CC 1-0 (Pharmacology)
Section cross-reference(s): 15, 63
REFERENCE COUNT: 114 THERE ARE 114 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 2 OF 22 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:514888 HCAPLUS
TITLE: Liposomal vasoactive intestinal peptide
AUTHOR(S): Sethi, Varun; Onyuksel, Hayat; Rubinstein, Israel
CORPORATE SOURCE: Departments of Pharmaceutics and Pharmacodynamics, University of Illinois at Chicago, Chicago, IL, 60612, USA
SOURCE: Methods in Enzymology (2005), 391, 377-395
CODEN: MENZAU; ISSN: 0076-6879
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Liposomes have been investigated as drug carriers since first discovered in the 1960s. However, the first-generation, so-called classic liposomes found relatively limited therapeutic utility. Nonetheless, the advent in the 1980s of the second-generation ste7rically stabilized liposomes (SSL) that evade uptake by the host's reticuloendothelial system greatly enhanced their utility as drug carriers because of their prolonged circulation half-life and passive targeting to injured and cancerous tissues. Over the past decade, our work focused on exploiting the bioactivity of vasoactive intestinal peptide (VIP), a ubiquitous 28-amino acid, amphipathic and pleiotropic mammalian neuropeptide, as a drug. To this end, the peptide expresses distinct and unique innate bioactivity that could be harnessed to treat several human diseases that represent unmet medical needs, such as pulmonary hypertension, stroke, Alzheimer's disease, sepsis, female sexual arousal dysfunction, acute lung injury, and arthritis. Unfortunately, the bioactive effects of VIP last only a few minutes due to its rapid degradation and inactivation by enzymes, **catalytic antibodies**, and spontaneous hydrolysis in biol. fluids. Hence, our goal was to develop and test stable, long-acting formulations of VIP using both classic and SSL as platform technologies. We found that spontaneous association of VIP with phospholipid bilayers leads

to a transition in the conformation of the peptide from random coil in an aqueous environment to α-helix, the preferred conformation for **ligand-receptor** interactions, in the presence of lipids. This process, in turn, protects VIP from degradation and inactivation and amplifies its bioactivity in vivo. Importantly, we discovered that the film rehydration and extrusion technique is the most suitable to passively load VIP onto SSL at room temperature and yields the most consistent results. Collectively, these attributes indicate that VIP on SSL represents a suitable formulation that could be tested in human disease.

CC 63 (Pharmaceuticals)
IT INDEXING IN PROGRESS
REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 3 OF 22 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:857331 HCAPLUS
DOCUMENT NUMBER: 141:346124
TITLE: Covalent attachment of ligands to nucleophilic proteins guided by non-covalent binding and applications for diagnosis, therapy, immunoassays and purification of recombinant proteins
INVENTOR(S): Paul, Sudhir; Nishiyama, Yasuhiro
PATENT ASSIGNEE(S): The University of Texas, USA
SOURCE: PCT Int. Appl., 144 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004087059	A2	20041014	WO 2004-US9399	20040326
WO 2004087059	A3	20050721		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2520392	AA	20041014	CA 2004-2520392	20040326
EP 1610808	A2	20060104	EP 2004-758449	20040326
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.:
US 2003-457293P P 20030326
WO 2004-US9399 W 20040326

AB A covalently reactive **ligand** analog (CAL) of formula [L1...Lx(L'-Y"-Y'-Y)...Lm]n: wherein, L1...Lx...Lm are components defining a **ligand** determinant, LX is a component unit of the **ligand** determinant selected from the group consisting of an amino acid residue, sugar residue, a fatty acid residue and a nucleotide, L' is a functional group of LX, Y' is atom, covalent bond or linker, Y' is an optional charged or neutral group Y is a covalently reactive electrophilic group that reacts specifically with a **receptor** that binds to

said **ligand** determinant, and n is an integer from 1 to 1000 m is an integer from 1 to 30.

IC ICM A61K

CC 9-10 (Biochemical Methods)
Section cross-reference(s): 1, 7, 15, 34, 63

IT Fibrillins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(1, **antibodies** to, NuR; covalent attachment of ligands to nucleophilic proteins guided by non-covalent binding and applications for diagnosis, therapy and immunoassays)

IT TCR (T cell **receptors**)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CD3 complex, NuR; covalent attachment of **ligands** to nucleophilic proteins guided by non-covalent binding and applications for diagnosis, therapy and immunoassays)

IT CD4 (antigen)
Epidermal growth factor **receptors**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NuR, activation or inactivation by conjugation with CAL; covalent attachment of **ligands** to nucleophilic proteins guided by non-covalent binding and applications for diagnosis, therapy and immunoassays)

IT **Antibodies** and Immunoglobulins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(alloantibodies, conjugates with CALs; covalent attachment of ligands to nucleophilic proteins guided by non-covalent binding and applications for diagnosis, therapy and immunoassays)

IT Epidermal growth factor **receptors**
Nucleic acids
Thyroglobulin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**antibodies** to, NuR; covalent attachment of **ligands** to nucleophilic proteins guided by non-covalent binding and applications for diagnosis, therapy and immunoassays)

IT Erythrocyte
Heart
Kidney
Lung
Platelet (blood)
(antigens, as NuR **antibodies**; covalent attachment of ligands to nucleophilic proteins guided by non-covalent binding and applications for diagnosis, therapy and immunoassays)

IT **Antibodies** and Immunoglobulins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(autoantibodies, conjugates with CALs; covalent attachment of ligands to nucleophilic proteins guided by non-covalent binding and applications for diagnosis, therapy and immunoassays)

IT **Antibodies and Immunoglobulins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**catalytic**, monoclonal, inhibition of by VIP-CAL; covalent attachment of ligands to nucleophilic proteins guided by non-covalent binding and applications for diagnosis, therapy and immunoassays)

IT **Antibodies** and Immunoglobulins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);

PREP (Preparation); USES (Uses)
(conjugates with CALs; covalent attachment of ligands to nucleophilic proteins guided by non-covalent binding and applications for diagnosis, therapy and immunoassays)

IT **Antibodies** and Immunoglobulins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(covalent attachment of ligands to nucleophilic proteins guided by non-covalent binding and applications for diagnosis, therapy and immunoassays)

IT Growth hormone **receptors**
VIP **receptors**
RL: BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(covalent attachment of **ligands** to nucleophilic proteins guided by non-covalent binding and applications for diagnosis, therapy and immunoassays)

IT Epidermal growth factor **receptors**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(extracellular, exEGFR, biotinylated, conjugate with PAR 4; covalent attachment of **ligands** to nucleophilic proteins guided by non-covalent binding and applications for diagnosis, therapy and immunoassays)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleophilic **receptors**, NuRs, conjugates with CALs; covalent attachment of **ligands** to nucleophilic proteins guided by non-covalent binding and applications for diagnosis, therapy and immunoassays)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleophilic **receptors**, NuRs; covalent attachment of **ligands** to nucleophilic proteins guided by non-covalent binding and applications for diagnosis, therapy and immunoassays)

IT **Antibodies** and Immunoglobulins
RL: BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(to HIV-1; covalent attachment of ligands to nucleophilic proteins guided by non-covalent binding and applications for diagnosis, therapy and immunoassays)

IT **Antibodies** and Immunoglobulins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(xenoantibodies, conjugates with CALs; covalent attachment of ligands to nucleophilic proteins guided by non-covalent binding and applications for diagnosis, therapy and immunoassays)

IT 9001-26-7, Prothrombin 37221-79-7, Vasoactive intestinal polypeptide 113189-02-9, Blood coagulation factor VIII
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**antibodies** to, NuR; covalent attachment of ligands to nucleophilic proteins guided by non-covalent binding and applications for diagnosis, therapy and immunoassays)

IT 7440-42-8DP, Boron, conjugates 7440-44-0DP, Carbon, conjugates 7440-62-2DP, Vanadium, conjugates 7723-14-0DP, Phosphorus, conjugates

548475-86-1DP, conjugates 548475-87-2DP, conjugates 548475-88-3DP, conjugates 552831-40-0P 775342-97-7DP, conjugate with Factor VIII via lysine side chains 775342-97-7DP, conjugate with biotinylated exEGFR and **antibodies** 775342-98-8DP, conjugates 775342-99-9DP, conjugates 776323-79-6DP, conjugates 776323-80-9DP, DNA conjugate
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(covalent attachment of ligands to nucleophilic proteins guided by non-covalent binding and applications for diagnosis, therapy and immunoassays)

L42 ANSWER 4 OF 22 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:203628 HCAPLUS
DOCUMENT NUMBER: 140:249204
TITLE: Adzymes comprising enzyme catalytic domains and targeting moieties and their uses
INVENTOR(S): Afeyan, Noubar B.; Baynes, Brian; Dasgupta, Ruchira; Lee, Frank D.; Wong, Gordon G.
PATENT ASSIGNEE(S): Compound Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 202 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004019878	A2	20040311	WO 2003-US26937		20030827
WO 2004019878	A3	20040715			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2497047	AA	20040311	CA 2003-2497047		20030827
US 2004081647	A1	20040429	US 2003-650591		20030827
EP 1539941	A2	20050615	EP 2003-791885		20030827
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2005537032	T2	20051208	JP 2004-569756		20030827
PRIORITY APPLN. INFO.:			US 2002-406517P	P	20020827
			US 2002-423754P	P	20021105
			US 2002-430001P	P	20021127
			WO 2003-US26937	W	20030827

AB Disclosed is a family of novel protein constructs, useful as drugs and for other purposes, termed 'adzymes,' comprising an targeting address moiety and a enzyme catalytic domain. In some types of disclosed adzymes, the address binds with a binding site on or in functional proximity to a targeted biomol., e.g., an extracellular targeted biomol., and is disposed adjacent the catalytic domain so that its affinity serves to confer anew specificity to the catalytic domain by increasing the effective local concentration of the target in the vicinity of the catalytic domain. The present

invention also provides pharmaceutical compns. comprising these adzymes, methods of making adzymes, DNA's encoding adzymes or parts thereof, and methods of using adzymes, such as for treating human subjects suffering from a disease, such as a disease associated with a soluble or membrane bound mol., e.g., an allergic or inflammatory disease. In a preferred embodiment of the invention, the substrate for an adzyme is **tumor necrosis factor** α (**TNF**α), such that a protease comprising the catalytic domain that decreases **TNF** α activity is selected from MT1-MMP, MMP12, tryptase, MT2-MMP, elastase, MMP7, chymotrypsin, and trypsin, and the targeting moiety is selected from a soluble portion of a **TNF**α receptor and a single-chain antibody that binds to **TNF**α.

IC ICM A61K
CC 7-8 (Enzymes)
Section cross-reference(s): 3, 15, 63
ST adzyme catalytic moiety fusion targeting moiety; **tumor necrosis factor** adzyme pharmaceutical; interleukin 1 adzyme pharmaceutical
IT **Antibodies and Immunoglobulins**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(monoclonal, targeting moiety; adzymes comprising enzyme **catalytic** domains and targeting moieties and their uses)
IT Molecular association
(**receptor-ligand**, modification of; adzymes comprising enzyme catalytic domains and targeting moieties and their uses)
IT Amyloid
Cytokines
Growth factors, animal
Hormones, animal, biological studies
Interleukin 1
Lipids, biological studies
Nucleic acids
Polysaccharides, biological studies
Prion proteins
Proteins
Receptors
Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(substrate; adzymes comprising enzyme catalytic domains and targeting moieties and their uses)
IT Agglutinins and Lectins
Antibodies and Immunoglobulins
Oligonucleotides
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(targeting moiety; adzymes comprising enzyme **catalytic** domains and targeting moieties and their uses)

L42 ANSWER 5 OF 22 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:722722 HCAPLUS
DOCUMENT NUMBER: 141:220884
TITLE: Selective protein degradation by ligand-targeted enzymes: catalytic antagonists
INVENTOR(S): Davis, Benjamin G.; Jones, John Bryan; Bott, Richard R.; Sanford, Karl John; Estell, David Aaron
PATENT ASSIGNEE(S): UK
SOURCE: U.S. Pat. Appl. Publ., 67 pp., Cont. of U.S. Ser. No.

566,466.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004170618	A1	20040902	US 2004-791628		20040301
PRIORITY APPLN. INFO.:			US 1999-161362P	P	19991026
			US 2000-566466	A1	20000508

AB This invention provides chimeric mols. that are catalytic antagonists of a target mol. The catalytic antagonists of this invention preferably comprise a targeting moiety attached to an enzyme that degrades the mol. specifically bound by the targeting moiety. The catalytic antagonists of this invention thus bind to a target recognized by the targeting moiety (e.g., a receptor) the enzyme component of the chimera then degrades all or part of the target. This typically results in a reduction or loss of activity of the target and release of the chimeric mol. The chimeric mol. is then free to attack and degrade another target mol. This invention also provides methods of enhancing the activity of a drug that acts as an inhibitor of a receptor or an enzyme. The methods involve coupling a hydrolase to said drug such that when said drug binds said receptor or enzyme, the hydrolase degrades the receptor or enzyme. In preferred embodiments, the method increases the dosage therapeutic window of said drug. Examples 1-4 demonstrate the highly specific selectivity of a catalytic antagonist of this invention in which the targeting moiety is a known enzyme inhibitor. Examples 5 through 7 detail the construction and evaluation of chimeric mols. in which the chimeric mols. are targeted to the binding protein lectin Con A. Examples 8 through 10 detail the construction and evaluation of chimeric mols. in which the chimeric mols. are targeted to the binding protein avidin. Examples 11 and 12 detail the construction and evaluation of chimeric mols. in which the chimeric mols. are targeted to a monoclonal anti-biotin antibody IgG. In this example, alc. dehydrogenase (ADH), which is strongly inhibited by 4-pyrazole derivs., was chosen as the target enzyme and the inhibitors chosen as targeting were pyrazoles known to inhibit ADH. A mutant of Bacillus lentus subtilisin (SBL) at S156C site was modified with 4-(6-methanethiosulfonyl)hexylpyrazole (MTS-pyrazole), and examined its targeting activity to horse liver alc. dehydrogenase (HLADH). In order to exploit the powerful binding of biotin to avidin as a model system to clearly demonstrate the targeting strategy the biotin-MTS reagent 1 was synthesized. As an extension of the targeted degradation of enzymes, the authors have focused on hapten-directed degradation of **antibodies** by SBL.

IC ICM A61K038-46
ICS C12N009-50
INCL 424094600; 435219000
CC 7-4 (Enzymes)
Section cross-reference(s): 6
IT **Antibodies and Immunoglobulins**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(IgG, monoclonal, conjugates, anti-biotin, chimeric mols. targeted to; selective protein degradation by ligand-targeted enzymes: **catalytic** antagonists)
IT Haptens
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES

(Uses)
(conjugates, with subtilisin, directed degradation of **antibodies** by; selective protein degradation by ligand-targeted enzymes: catalytic antagonists)

IT **Antibodies and Immunoglobulins**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(hapten directed degradation of, by SBL; selective protein degradation by ligand-targeted enzymes: **catalytic** antagonists)

IT **Receptors**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(target; selective protein degradation by **ligand**-targeted enzymes: catalytic antagonists)

L42 ANSWER 6 OF 22 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:702263 HCAPLUS
DOCUMENT NUMBER: 141:253488
TITLE: Agents in development for the management of cocaine abuse
AUTHOR(S): Gorelick, David A.; Gardner, Eliot L.; Xi, Zheng-Xiong
CORPORATE SOURCE: Intramural Research Program, National Institute on Drug Abuse, Department of Health and Human Services, National Institutes of Health, Baltimore, MD, USA
SOURCE: Drugs (2004), 64(14), 1547-1573
CODEN: DRUGAY; ISSN: 0012-6667
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Cocaine abuse is a serious health problem in many areas of the world, yet there are no proven effective medications for the treatment of cocaine dependence. Preclin. studies suggest that the reinforcing effect of cocaine that promotes its abuse is mediated by blockade of the presynaptic dopamine transporter. This results in increased dopamine activity in the mesolimbic or meso-accumbens dopamine reward system of brain. Development of new medications to treat cocaine dependence has focused on manipulation of this dopamine system, either by direct action on dopamine binding sites (transporter or **receptors**) or indirectly by affecting other neurotransmitter systems that modulate the dopamine system. In principle, a medication could act via one of three mechanisms: (i) as a substitute for cocaine by producing similar dopamine effects; (ii) as a cocaine antagonist by blocking the binding of cocaine to the dopamine transporter; or (iii) as a modulator of cocaine effects by acting at other than the cocaine binding site. The US National Institute on Drug Abuse has a Clin. Research Efficacy Screening Trial (CREST) program to rapidly screen existing medications. CREST identified four medications warranting phase II controlled clin. trials: cabergoline, reserpine, sertraline and tiagabine. In addition, disulfiram and selegiline (deprenyl) have been effective and well tolerated in phase II trials. However, selegiline was found ineffective in a recent phase III trial. Promising existing medications probably act via the first or third aforementioned mechanisms. Sustained-release formulations of stimulants such as methylphenidate and amfetamine (amphetamine) have shown promise in a stimulant substitution approach. Disulfiram and selegiline increase brain dopamine concns. by inhibition of dopamine-catabolizing enzymes (dopamine-β-hydroxylase and monoamine oxidase B, resp.). Cabergoline is a direct dopamine **receptor** agonist, while reserpine depletes presynaptic stores of dopamine (as well as norepinephrine and serotonin). Sertraline, baclofen and vigabatrin indirectly reduce dopamine activity by

increasing activity of neurotransmitters (serotonin and GABA) that inhibit dopamine activity. Promising new medications act via the second or third aforementioned mechanisms. Vanoxerine is a long-acting inhibitor of the dopamine transporter which blocks cocaine binding and reduces cocaine self-administration in animals. Two dopamine **receptor ligands** that reduce cocaine self-administration in animals are also undergoing phase I human safety trials. Adrogolide is a selective dopamine D1 **receptor** agonist; BP 897 is a D3 **receptor** partial agonist. A pharmacokinetic approach to treatment would block the entry of cocaine into the brain or enhance its catabolism so that less cocaine reached its site of action. This is being explored in animals using the natural cocaine-metabolizing enzyme butyrylcholinesterase (or recombinant versions with enhanced capabilities), **catalytic antibodies**, and passive or active immunization to produce anti-cocaine binding antibodies. A recent phase I trial of a 'cocaine vaccine' found it to be well tolerated and producing detectable levels of anti-cocaine antibodies for up to 9 mo after immunization.

CC 1-0 (Pharmacology)
REFERENCE COUNT: 256 THERE ARE 256 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 7 OF 22 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:570727 HCAPLUS
DOCUMENT NUMBER: 139:111652
TITLE: Method for the treatment of asthma
INVENTOR(S): Arndt, Gregory Martin; Black, Judith Lee; Hunt, Nicholas Henry; Burgess, Janette Kay; Pack, Robert Andrew
PATENT ASSIGNEE(S): J & J Research Pty Ltd, Australia
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003059245	A2	20030724	WO 2002-IB5824	20021217
WO 2003059245	A3	20040603		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004009174	A1	20040115	US 2002-321145	20021217
PRIORITY APPLN. INFO.:			US 2001-341453P	P 20011218

AB A method is disclosed for the treatment of asthma. The invention relates to methods for inhibiting the binding of OX40 and OX40L in smooth muscle cells to reduce inflammatory responses in smooth muscle containing tissue.

IC ICM A61K
CC 1-7 (Pharmacology)
Section cross-reference(s): 15, 34

IT **Receptors**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(0X40 for OX40L (OX40 **ligand**); method for treatment of asthma)
IT **Antibodies and Immunoglobulins**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**catalytic**; method for treatment of asthma)
IT **Antibodies** and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(intracellular; method for treatment of asthma)
IT **Antibodies** and Immunoglobulins
CD40 (antigen)
Interleukin 6
Tumor necrosis factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method for treatment of asthma)
IT **Antibodies** and Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(monoclonal, and fragments thereof, specifically binding to OX40 or OX40L; method for treatment of asthma)
IT **Antibodies** and Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(recombinant and fragments of; method for treatment of asthma)

L42 ANSWER 8 OF 22 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:8172 HCAPLUS
DOCUMENT NUMBER: 142:296676
TITLE: Multifunctional ligands or **antibodies** for immunotherapy of immune disease, autoimmune disease, transplant rejection, infection and cancer
INVENTOR(S): Herman, William
PATENT ASSIGNEE(S): Can.
SOURCE: Can. Pat. Appl., 107 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2365636	AA	20030605	CA 2001-2365636	20011205
PRIORITY APPLN. INFO.:			CA 2001-2365636	20011205

AB The present invention relates to heterofunctional **ligand** comprising first and second moieties which have cooperating functional affinities as well as a functional **ligand**. For example, the **ligand** is a bispecific antibody having at least a first portion which binds to a lymphatic vessel-associated antigen or **receptor** and a second portion having at least one immune-affecting functionality related to e.g. antigen presentation, immune signalling, suppression of enhancement of immune tolerance or immunostimulation, or binding to a target mol. such as a cell surface antigen, **receptor**, etc.
IC ICM A61K039-395
ICS A61K045-00; A61K047-48
CC 15-3 (Immunochemistry)
Section cross-reference(s): 3, 63
IT Chemokine **receptors**

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CCR5; multifunctional **ligands** or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT CD antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD102; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT CD antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD106; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD134; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT CD antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD18; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Glycoproteins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD40-L (antigen CD40 ligand); multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD49a; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT CD antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CD54; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Inflammation
(Crohn's disease; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Intestine, disease
(Crohn's; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Selectins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E-; multifunctional ligands or **antibodies** for immunotherapy

of autoimmune disease, transplant rejection, infection and cancer)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(H11; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ICAM (intercellular adhesion mol.); multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ICAM-1 (intercellular adhesion mol. 1); multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ICAM-2 (intercellular adhesion mol. 2); multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT **Antibodies** and Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(IgG; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT **Receptors**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LYVE-1 (lymphatic vessel endothelial hyaluronan **receptor** 1); multifunctional **ligands** or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Leu-CAM (leukocytic cell adhesion mol.); multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Antigens
Receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Lymph vessel-associated; multifunctional **ligands** or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MAdCAM-1 (mucosal addressin cell adhesion mol.-1); multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(MHC (major histocompatibility complex), class I; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MHC (major histocompatibility complex), class II; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Histocompatibility antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MHC (major histocompatibility complex); multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Ligands
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(OX40; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Tumor antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(TAG-72 (tumor-associated glycoprotein 72); multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Cell adhesion molecules
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(VCAM-1 (vascular cell adhesion mol. 1); multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT B cell (lymphocyte)
Leukocyte
Lymphocyte
T cell (lymphocyte)
(activation; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Carcinoma
(adenocarcinoma; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Leukocyte
(adhesion; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT **Antibodies** and Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(anti-idiotypic; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Camelus
(antibody; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT **Antibodies** and Immunoglobulins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(autoantibodies; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(autoantigens; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT **Antibodies** and Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bispecific; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Drug delivery systems
(carriers; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT **Antibodies and Immunoglobulins**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**catalytic**; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT **Antibodies** and Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chimeric; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-stimulatory; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Carcinoma
(colon adenocarcinoma; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Intestine, neoplasm
(colon, adenocarcinoma; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT **Antibodies** and Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conjugates; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Toxins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(cytotoxins; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Immunity
(disorder; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Ribosome
(display library; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT DNA
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(double-stranded; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT **Antibodies** and Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fragments; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Carcinoma
(hepatocellular; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Liver, neoplasm
(hepatoma; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT **Antibodies** and Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(humanized; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Signal transduction, biological
(immune; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Drug delivery systems
(immunoconjugates; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Drug delivery systems
(immunotoxins; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Interleukin **receptors**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(interleukin 12; multifunctional **ligands** or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Cell activation

(leukocyte; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Drug delivery systems
(liposomes; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Lymphatic system
(lymph vessel, endothelium; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Lymphatic system
(lymph vessel; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Endothelium
(lymphatic; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT **Antibodies** and Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Affinity
Antigen presentation
Antitumor agents
Apoptosis
Autoimmune disease
B cell (lymphocyte)
Biomarkers
Carcinoma
Cell migration
Drugs
Epitopes
Human
Immune tolerance
Immunity
Immunostimulation
Immunosuppression
Immunotherapy
Infection
Leukemia
Lymphoma
Molecules
Neoplasm
Phage display library
T cell (lymphocyte)
Transplant rejection
(multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT **Antibodies** and Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Avidins
CD2 (antigen)
CD22 (antigen)
CD28 (antigen)
CD3 (antigen)
CD30 (antigen)
CD38 (antigen)
CD4 (antigen)
CD40 (antigen)
CD44 (antigen)
CD5 (antigen)
CD69 (antigen)
CD8 (antigen)
CD80 (antigen)
CD86 (antigen)
CTLA-4 (antigen)
Carcinoembryonic antigen
Cell adhesion molecules
Chemokine **receptors**
Chemokines
Cytokine **receptors**
Cytokines
Epidermal growth factor **receptors**
Fas antigen
Fusion proteins (chimeric proteins)
G protein-coupled **receptors**
Growth factor **receptors**
Growth factors, animal
Insulin-like growth factor II **receptors**
Interleukin 2 **receptors**
Interleukin 6 **receptors**
LFA-1 (antigen)
LFA-3 (antigen)
Notch (**receptor**)
RNA
Radionuclides, biological studies
Selectins
Toxins
Tumor antigens
Tumor necrosis factor receptors
Tumor necrosis factors
Tyrosine kinase **receptors**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(multifunctional **ligands** or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT Ligands
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(multifunctional; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

IT **Antibodies** and Immunoglobulins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(polyclonal; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection

and cancer)
IT Antigens
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(surface, cell; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)
IT Lupus erythematosus
(systemic; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)
IT Vaccines
(tumor; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)
IT Antitumor agents
(vaccines; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)
IT Infection
(viral; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)
IT Interleukin 2 **receptors**
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α chain; multifunctional **ligands** or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)
IT Integrins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β1; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)
IT 127464-60-2, VEGF
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(2; multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)
IT 9001-99-4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(multifunctional ligands or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)
IT 58-85-5, Biotin 9013-20-1, Streptavidin 54249-88-6, Antigens, CD26
340700-49-4, **Receptor** serine kinase
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(multifunctional **ligands** or **antibodies** for immunotherapy of autoimmune disease, transplant rejection, infection and cancer)

L42 ANSWER 9 OF 22 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:114029 HCAPLUS
DOCUMENT NUMBER: 136:147491
TITLE: Detection of binding reactions using labels detected by mediated catalytic electrochemistry
INVENTOR(S): Stewart, David H.; Groelke, John W.; Thorp, H. Holden; Eckhardt, Allen E.

PATENT ASSIGNEE(S): Xanthon, Inc., USA; The University of North Carolina At Chapel Hill
SOURCE: U.S., 25 pp., Cont.-in-part of U.S. Ser. No. 603,217. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6346387	B1	20020212	US 2000-722065	20001124
US 5871918	A	19990216	US 1996-667338	19960620
EP 1193315	A1	20020403	EP 2001-130632	19960624
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6132971	A	20001017	US 1998-179665	19981027
US 6180346	B1	20010130	US 1999-267552	19990312
US 6361951	B1	20020326	US 2000-603217	20000626
AU 753350	B2	20021017	AU 2000-53462	20000817
WO 2002042771	A2	20020530	WO 2001-US21571	20010709
WO 2002042771	A3	20020912		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001071919	A5	20020603	AU 2001-71919	20010709
US 2002106683	A1	20020808	US 2001-8233	20011106
US 2002037530	A1	20020328	US 2001-991015	20011116
JP 2004117371	A2	20040415	JP 2003-375926	20031105
US 2004241738	A1	20041202	US 2004-884299	20040702
JP 2004357714	A2	20041224	JP 2004-213311	20040721
US 2005233358	A1	20051020	US 2005-72388	20050304

PRIORITY APPLN. INFO.:	US 1995-495817	B2 19950627
	US 1995-60949P	P 19950627
	US 1996-667338	A3 19960620
	US 1998-179665	A3 19981027
	US 1999-267552	A2 19990312
	US 2000-603217	A2 20000626
	US 1996-16265P	P 19960419
	US 1996-667337	A2 19960620
	EP 1996-922533	A3 19960624
	JP 1997-504485	A3 19960624
	US 1997-950503	A2 19971014
	US 2000-722065	A 20001124
	WO 2001-US21571	W 20010709
	US 2001-8233	A1 20011106
	US 2001-991015	A1 20011116

AB The invention concerns a method of detecting binding interactions and target mols., such as proteins, protein fragments, recombinant proteins, recombinant protein fragments, extracellular matrix proteins, **ligands**, carbohydrates, steroids, hormones, drugs, drug candidates, Igs and **receptors** of eukaryotic, prokaryotic or

viral origin, by mediated electrochem. using labels that react with transition metal mediator complexes in a detectable catalytic redox reaction. These labels are attached directly to binders, target mols., surrogate target mols., or to affinity **ligands** capable of binding to the target or to surrogate target mols. capable of competing with the target for binding to another binder. The labels can be naturally present (endogenous) in the binder, target or affinity **ligand**, or constructed by the covalent attachment of the label to the binder, target, affinity **ligand** or surrogate target (exogenous).

IC ICM C12Q001-68
ICS C12P019-34; C07H021-02; A61B005-05
INCL 435006000
CC 9-14 (Biochemical Methods)
IT **Antibodies and Immunoglobulins**
RL: ANT (Analyte); ANST (Analytical study)
(IgG; detection of binding reactions using labels detected by mediated **catalytic** electrochem.)
IT Amino acids, uses
Antibodies and Immunoglobulins
Oligonucleotides
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(detection of binding reactions using labels detected by mediated **catalytic** electrochem.)
IT **Antibodies and Immunoglobulins**
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(detection of binding reactions using labels detected by mediated **catalytic** electrochem.)
REFERENCE COUNT: 117 THERE ARE 117 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 10 OF 22 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:683770 HCAPLUS
DOCUMENT NUMBER: 130:79521
TITLE: Proteinase requirements of epidermal growth factor-induced ovarian cancer cell invasion
AUTHOR(S): Ellerbroek, Shawn M.; Hudson, Laurie G.; Stack, M. Sharon
CORPORATE SOURCE: Departments of Obstetrics & Gynecology and Cell & Molecular Biology, Northwestern University Medical School, Chicago, IL, USA
SOURCE: International Journal of Cancer (1998), 78(3), 331-337
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Aberrant expression or activity of the epidermal growth factor (EGF) **receptor** family of tyrosine kinases has been associated with tumor progression and an invasive phenotype. In this study, the authors utilized 4 ovarian cancer cell lines, OVCA 432, DOV 13, OVEA6 and OVCA 429, to determine the effects of EGF on the regulation of proteolytic enzymes and their inhibitors, cellular migration and in vitro invasion. Induction of urinary-type plasminogen activator (u-PA) activity and tissue inhibitor of matrix metalloproteinase (TIMP)-1 was observed in all 4 cell lines. OVCA 432 cells showed strong PAI-1 induction; however, the other 3 lines displayed substantial baseline PAI-1 expression that was not induced by EGF. EGF-dependent stimulation of migration and induction of matrix

metalloproteinase (MMP)-9 (gelatinase B) was observed in OVEA6 and OVCA 429 cells only. Upon EGF **receptor** activation, DOV 13, OVEA6 and OVCA 429 cells were induced to invade through an artificial basement membrane (Matrigel); however, no invasion was detected in OVCA 432 cells. Cell lines displaying induction of migration and MMP-9 (OVEA6 and OVCA 429) demonstrated robust EGF-induced invasion (5- to 20-fold), and cell invasion was substantially reduced in the presence of anti-**catalytic** MMP-9 **antibody**. Addition of anti-**catalytic** u-PA **antibody** inhibited the modest (<2-fold) EGF-induced invasion in a cell line that did not express MMP-9 (DOV 13) and in OVEA6 cells that displayed the highest baseline u-PA activity. Together, the findings indicate that multiple proteinases are important in ovarian cell invasion and implicate EGF induction of MMP-9 and migration as key components of more aggressive **ligand**-induced invasion.

CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 11 OF 22 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:316769 HCAPLUS
DOCUMENT NUMBER: 122:72695
TITLE: Biological activation of pro-HGF (hepatocyte growth factor) by urokinase is controlled by a stoichiometric reaction
AUTHOR(S): Naldini, Luigi; Vigna, Elisa; Bardelli, Alberto; Follenzi, Antonia; Galimi, Francesco; Comoglio, Paolo M.
CORPORATE SOURCE: Dep. Biomed. Sci. Oncol., Univ. Torino Med. Sch., Torino, 10126, Italy
SOURCE: Journal of Biological Chemistry (1995), 270(2), 603-11
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hepatocyte growth factor (HGF) is a paracrine inducer of morphogenesis and invasive growth in epithelial and endothelial cells. HGF is secreted by mesenchymal cells as an inactive precursor (pro-HGF). The crucial step for HGF activation is the extracellular hydrolysis of the Arg494-Val495 bond, which converts pro-HGF into αβ-HGF, the high-affinity **ligand** for the Met **receptor**. The authors previously reported that the urokinase-type plasminogen activator (uPA) activates pro-HGF in vitro. The authors now show that this is a stoichiometric reaction, and provide evidence for its occurrence in tissue culture. Activation involves the formation of a stable complex between pro-HGF and uPA. This complex was isolated from the in vitro reaction of pure uPA with recombinant pro-HGF, as well as from the membrane of target cells, after sequential addition of uPA and pro-HGF. On the cell membrane, the uPA·HGF complex was bound to the Met **receptor**. Monocytic cell lines, and primary monocytes after adhesion, activated efficiently pro-HGF both on their surface and in the culture medium. This activation was inhibited by anti-**catalytic** anti-uPA **antibodies**, and occurred by a stoichiometric reaction. The stoichiometry of the activation reaction suggests that the biol. effects of HGF can be titrated in vivo by the level of uPA activity. Adequate amts. of uPA can be locally provided by the macrophages, which would condition the tissue microenvironment by rendering HGF bioavailable to its target cells.

CC 2-10 (Mammalian Hormones)

L42 ANSWER 12 OF 22 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:621462 HCAPLUS
DOCUMENT NUMBER: 121:221462
TITLE: Urokinase-type plasminogen activator enhances invasion of human T cells (Jurkat) into a fibrin matrix
AUTHOR(S): Kramer, Michael D.; Spring, Herbert; Todd, Robert F.; Vettel, Ulrike
CORPORATE SOURCE: Institute for Immunology and Serology, University of Heidelberg, Heidelberg, D-69120, Germany
SOURCE: Journal of Leukocyte Biology (1994), 56(2), 110-16
CODEN: JLBIE7; ISSN: 0741-5400
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **receptor** for urokinase-type plasminogen activator (uPA-R) localizes uPA to the cell surface. The **receptor**-bound uPA converts plasminogen to the trypsin-like endopeptidase plasmin. Thus uPA is involved in the initiation of pericellular proteolysis. Pericellular proteolysis is assumed to facilitate the cellular infiltration into surrounding tissue. The uPA-R has recently been identified as a surface antigen of activated human T lymphocytes. We have characterized the uPA-R of the human CD4+ T cell line Jurkat by immunol. (flow cytometry), biochem. (**ligand** blotting), and physico-chemical (Scatchard blotting) methods. The collective data suggest that the human CD4+ T cell line Jurkat expresses a cell surface **receptor** for uPA similar to that of myelo/monocytes and normal T cells with regard to size, affinity, **ligand** specificity, and antigenicity. Binding studies using exogenous uPA and subsequent functional assays revealed that **receptor**-bound uPA retains its enzymic activity. Saturation of the Jurkat cell uPA-R with exogenous uPA facilitated cellular invasion into fibrin matrixes in vitro. UPA-dependent invasion was inhibited in the presence of an anti-**catalytic** monoclonal anti-uPA **antibody**. We propose that uPA-R-bound uPA may facilitate the invasiveness of uPA-R-pos. T lymphocytes.
CC 1-8 (Pharmacology)

L42 ANSWER 13 OF 22 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:470363 HCAPLUS
DOCUMENT NUMBER: 119:70363
TITLE: Molecules with antibody combining sites that catalyze glycosidic reactions
INVENTOR(S): Tramontano, Alfonso; Janjic, Nebojsa
PATENT ASSIGNEE(S): Scripps Research Institute, USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9306838	A1	19930415	WO 1992-US8324	19920930
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
PRIORITY APPLN. INFO.:			US 1991-771040 A	19911002

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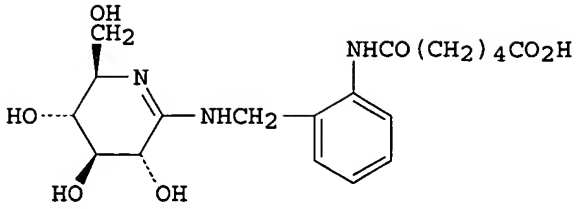


I

AB Monoclonal antibodies or paratope-containing portions thereof (monoclonal **receptors**) that hydrolyze a specific glycosidic bond of a reactant **ligand** glycoside are disclosed, as are methods for preparing the monoclonal **receptor** mols. Thus, I was prepared and conjugated with albumin, and the conjugate was used as an **immunogen** in a standard protocol for hybridoma production In a glycosidase activity assay, 1 of the produced monoclonal **receptors** (8D11) showed a rate of 3.4 x 10-6 M/h, or better than double the background rate. The activity was shown to be specific for the α-glucoside, and no acceleration over background was observed for any clone with the β-glucoside.

IC ICM A61K035-16
ICS C12N015-00; C12N005-00

CC 15-3 (Immunochemistry)
Section cross-reference(s): 7, 33

ST monoclonal **catalytic antibody** glycoside hydrolysis

IT Glycosides
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrolysis of, monoclonal **catalytic antibody** for)

IT Hydrolysis
(of glycosidic bonds, monoclonal **catalytic antibody** for)

IT **Antibodies**
RL: BIOL (Biological study)
(**catalytic**, monoclonal, glycoside hydrolysis with)

IT 34246-15-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrolysis of, monoclonal **catalytic antibody** for)

IT 9032-92-2, Glycosidase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(monoclonal **catalytic antibody** with activity of)

IT 77162-04-0P 77174-08-4P 148891-54-7P 148891-55-8P 148891-56-9P 148913-32-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in **immunogen** preparation for glycosidic bond-hydrolyzing monoclonal **catalytic antibody** production)

IT 148913-33-1DP, albumin conjugates
RL: PREP (Preparation)
(preparation of, for **immunogen** for glycosidic bond-hydrolyzing monoclonal **catalytic antibody** production)

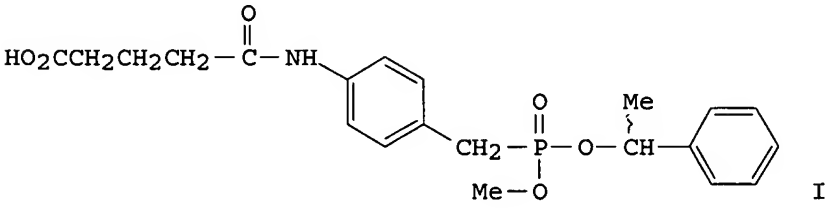
IT 14904-83-7P 134735-73-2P 148913-33-1P
RL: PREP (Preparation)
(preparation of, in **immunogen** preparation for glycosidic bond-hydrolyzing monoclonal **catalytic antibody**

production)
IT 128732-72-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in **immunogen** preparation for glycosidic bond-hydrolyzing monoclonal **catalytic antibody** production)

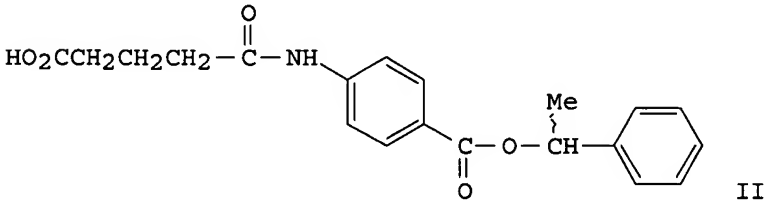
L42 ANSWER 14 OF 22 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:205394 HCAPLUS
DOCUMENT NUMBER: 114:205394
TITLE: Receptor molecules containing antibody combining sites that exhibit stereospecifically catalyzed hydrolysis of carboxylic acid amide or ester bonds
INVENTOR(S): Lerner, Richard; Janda, Kim; Benkovic, Stephen
PATENT ASSIGNEE(S): Scripps Clinic and Research Foundation, USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9008185	A1	19900726	WO 1990-US269	19900112
W: AU, DK, FI, JP, KR, NO				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
AU 9050382	A1	19900813	AU 1990-50382	19900112
AU 650846	B2	19940707		
EP 454778	A1	19911106	EP 1990-902870	19900112
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 04502708	T2	19920521	JP 1990-503094	19900112
CA 2007816	AA	19900717	CA 1990-2007816	19900116
NO 9102786	A	19910912	NO 1991-2786	19910716
FI 95928	B	19951229	FI 1991-3427	19910716
FI 95928	C	19960410		

PRIORITY APPLN. INFO.: US 1989-297798 A 19890117
WO 1990-US269 A 19900112
OTHER SOURCE(S): MARPAT 114:205394
GI



I



II

AB A **receptor** mol. for catalytically hydrolyzing a predetd. scissile carboxylic acid amide or ester bond of a reactant-**ligand** stereoisomer contains an antibody combining site which binds to: (a) 1 of a pair of the reactant-**ligand** stereoisomers that contains the predetd. scissile carboxylic acid amide or ester bond; and (b) 1 of a pair of analog-**ligand** stereoisomers that is stereochem. analogous to the reactant **ligand** and that contains a tetrahedrally bonded P at a position analogous to that of the scissile carbonyl C of the predetd. carboxylic acid amide or ester bond. The **receptor** mol. is an antibody or its fragment. Phosphonic diester I was prepared and linked to keyhole limpet hemocyanin to be used as an **immunogenic** conjugate to immunize mice. Hybridomas were then prepared using spleen cells from the immunized mice. Twelve hybridomas secreted monoclonal antibodies which bound to I coupled to bovine serum albumin in an ELISA. Each of those binding interactions was inhibited by preincubation of the **receptor** with free I in solution, thereby indicating the interactions were specific to the bound haptenic analog-**ligand**. Of those 12 monoclonal **antibodies**, 8 can **catalytically** hydrolyze the R-(+) or S-(-) isomer of the ester reactant-**ligand** II. Of the 8, 2 catalyzed the hydrolysis of only the S-(-) isomer reactant-**ligand**, whereas the other 6 catalyzed the hydrolysis of only the R-(+) reactant-**ligand** II.

IC ICM C12N005-12
ICS C12N009-16; C12N009-78; C12N009-80

CC 15-3 (Immunochemistry)

ST **receptor** reactant **ligand** analog binding; amide hydrolysis antibody stereospecific catalysis; ester hydrolysis antibody stereospecific catalysis

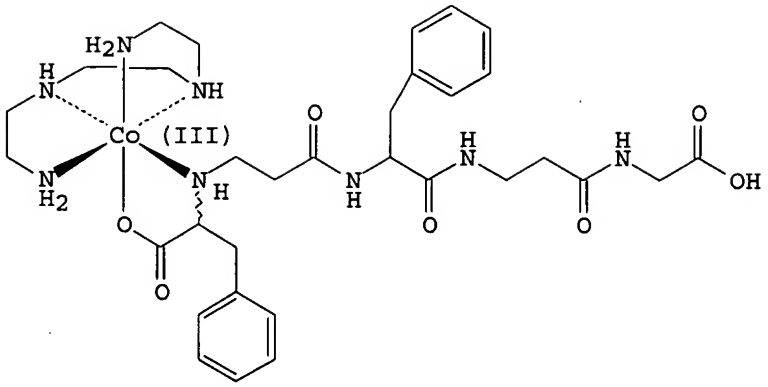
L42 ANSWER 15 OF 22 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:162305 HCAPLUS
DOCUMENT NUMBER: 114:162305
TITLE: Antibody-combining-site-containing receptor molecule binding to metal ion coordination complex for catalysis of peptide hydrolysis
INVENTOR(S): Iverson, Brent L.; Lerner, Richard A.
PATENT ASSIGNEE(S): Scripps Clinic and Research Foundation, USA
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9007934	A1	19900726	WO 1990-US235	19900112
W: AU, DK, FI, JP, KR, NO				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
US 5236825	A	19930817	US 1989-298082	19890117
AU 9049632	A1	19900813	AU 1990-49632	19900112
AU 650419	B2	19940623		
EP 454766	A1	19911106	EP 1990-902491	19900112
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 04504526	T2	19920813	JP 1990-502848	19900112
CA 2007818	AA	19900717	CA 1990-2007818	19900116
NO 9102785	A	19910912	NO 1991-2785	19910716
PRIORITY APPLN. INFO.:			US 1989-298082 A	19890117

WO 1990-US235 A 19900112

GI



I

AB A receptor mol. containing an antibody-combining-site which immunol. binds to a polyvalent metal ion-containing coordination complexes is disclosed. The coordination complex of a 1st immunoligand is kinetically inert, whereas that of a 2nd immunoligand is kinetically labile. The receptor mol. can catalyze a reaction of the 2nd immunoligand (e.g. hydrolysis of a predetd. peptide bond). The receptor mol. is a biol. active mol. containing an antibody-combining-site, i.e. a monoclonal antibody or its fragment, which can be prepared by a standard hybridoma method using the 1st immunoligand as **immunogen**. A relatively kinetically inert Co(III) moiety was complexed to a synthesized tetrapeptide to form coordination complex I and conjugated with keyhole limpet hemocyanin. The conjugate was then used as an **immunogen** to prep monoclonal antibodies by a standard hybridoma method. Thirteen hybridomas secreted monoclonal antibodies which were specific to coordination complex I as determined by ELISA. Each of the 13 monoclonal antibodies exhibited peptide bond cleavage (amide hydrolysis) activity with 6 different substrate peptides using several different trien metal complexes as cofactors for the immunoligand formed. A rapid and sensitive assay for detection of the free amine groups released by peptide hydrolysis was also given.

IC ICM A61K039-00
ICS A61K035-14; C07K003-00; C07K013-00; C07K015-00; C07K017-00; G01N033-563; C12N005-00

CC 15-3 (Immunochemistry)

IT **Antibodies**
RL: CAT (Catalyst use); USES (Uses)
(**catalytic**, monoclonal, peptide-hydrolyzing, in presence of metal complex as cofactor for immunoligand)

IT **Ligands**
RL: RCT (Reactant); RACT (Reactant or reagent)
(complexes, polyvalent metal ion-containing, antibody-combining-site **receptor** mol. binding to, in monoclonal abzyme preparation and peptide hydrolysis)

IT 7429-90-5D, Aluminum, peptide complexes 7439-89-6D, Iron, peptide complexes 7439-94-3D, Lutetium, peptide complexes 7439-95-4D, Magnesium, peptide complexes 7439-96-5D, Manganese, peptide complexes 7440-02-0D, Nickel, peptide complexes 7440-48-4D, Cobalt, peptide complexes, hemocyanin conjugates 7440-50-8D, Copper, peptide complexes 7440-55-3D, Gallium, peptide complexes 7440-66-6D, Zinc, peptide

complexes 7440-74-6D, Indium, peptide complexes
RL: RCT (Reactant); RACT (Reactant or reagent)
(as **immunogen** in preparation of monoclonal abzymes for catalysis of peptide hydrolysis)
IT 120534-51-2D, conjugates with keyhole limpet hemocyanin
RL: RCT (Reactant); RACT (Reactant or reagent)
(as **immunogen** in preparation of peptide-hydrolyzing monoclonal abzymes)
IT 31240-97-8P 35322-60-2P 132952-73-9DP, resin-bound 132952-74-0DP, resin-bound 132952-74-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, in preparation of **immunogen** for preparation of peptide-hydrolyzing monoclonal abzymes)
IT 156-06-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with synthetic peptide, in preparation of **immunogen** for preparation of peptide-hydrolyzing monoclonal abzymes)

L42 ANSWER 16 OF 22 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:613220 HCAPLUS
DOCUMENT NUMBER: 111:213220
TITLE: Antibody combining sites that exhibit stereoselective synthase activity, and their use in ester and amide synthesis and stereoisomer separation
INVENTOR(S): Benkovic, Stephen; Lerner, Richard A.; Tramontano, Alfonso; Napper, Andrew D.
PATENT ASSIGNEE(S): Scripps Clinic and Research Foundation, USA
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8809380	A1	19881201	WO 1988-US1766	19880526
W: AU, DK, FI, JP, NO				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4900674	A	19900213	US 1987-55177	19870528
US 5079152	A	19920107	US 1987-83681	19870807
AU 8819457	A1	19881221	AU 1988-19457	19880526
AU 632459	B2	19930107		
EP 315680	A1	19890517	EP 1988-905508	19880526
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 02500162	T2	19900125	JP 1988-505163	19880526
DK 8900319	A	19890125	DK 1989-319	19890125
NO 8900366	A	19890322	NO 1989-366	19890127
NO 176058	B	19941017		
NO 176058	C	19950125		
FI 8900450	A	19890130	FI 1989-450	19890130
US 5248611	A	19930928	US 1992-816956	19920103

PRIORITY APPLN. INFO.: US 1987-55177 A 19870528
US 1987-83681 A 19870807
WO 1988-US1766 A 19880526
OTHER SOURCE(S): MARPAT 111:213220
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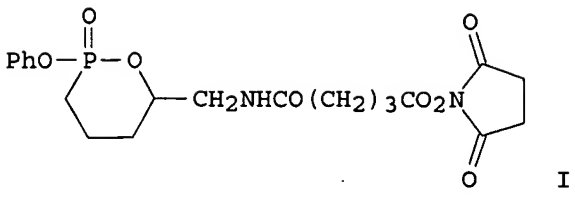

I

AB A P-containing analog-**ligand** having a steric configuration that substantially corresponds to the configuration of an amide- or ester-forming transition state is used to induce production of **receptor** mols. whose antibody combining sites have stereospecific amide or ester (especially lactam or lactone) synthase catalytic activity when reacted with a **ligand** containing (a) a carbonyl C atom and (b) an amine or alc. group that are structurally capable of forming a preselected stereoisomer of a carboxylic amide or ester. Methods for other stereoselective syntheses and for separation of stereoisomers with **receptor** mols. containing appropriate antibody combining sites are described. The amide (I) formed from 2-phenoxy-2-oxo-6-aminomethyl-1,2-oxaphosphorinane and glutaryl chloride N-hydroxysuccinimide ester was conjugated with keyhole limpet hemocyanin and used to immunize mice for formation of monoclonal antibody 24B11 to I by the standard hybridoma technique, screening for both antibody and hydrolytic activity. This antibody was active as a lactone synthase on Ph 6-acetamido-5-hydroxyhexanoate as substrate; the reaction was inhibited by the I analog 2-phenoxy-2-oxo-6-(acetamidomethyl)-1,2-oxaphosphorinane (II). Half of the substrate was rapidly transformed by the antibody, as expected for stereospecific synthesis where only 1 enantiomer of the substrate is bound. I was prepared in 7 steps, including cyclization of Ph iso-Pr 4-pentenylphosphonate with I2 to 2-phenoxy-2-oxo-6-iodomethyl-1,2-oxaphosphorinane.

IC ICM C12P017-06
ICS C12N009-00; C12N009-88; C07K015-06

CC 15-3 (Immunochemistry)
Section cross-reference(s): 7, 9, 27, 28

ST antibody combining site enzyme activity; lactone synthase activity monoclonal antibody; oxaphosphorinane prepn monoclonal antibody; stereoselective synthesis antibody; enantiomer sepn antibody; **catalytic antibody** ester amide prepn

IT Kinetics of lactonization
(by **catalytic antibody**)

IT Transition state structure
(in lactonization, **catalytic antibody** to)

IT Kinetics, enzymic
Michaelis constant
(of **catalytic antibody** with lactone synthase activity)

IT Amides, preparation
Esters, preparation
RL: PREP (Preparation)
(preparation of, stereoselective **catalytic antibodies** for)

IT **Antibodies**
RL: BIOL (Biological study)
(**catalytic**, stereoselective, amide and ester formation with)

IT **Antibodies**
RL: BIOL (Biological study)

(**catalytic**, monoclonal, stereoselective, amide and ester formation with)
IT Hemocyanins
RL: BIOL (Biological study)
(conjugates, with lactonization transition state analogs, for **catalytic antibody** production)
IT 13598-36-2D, Phosphonic acid, derivs.
RL: BIOL (Biological study)
(**antibodies** to, **catalytic**, amide and ester formation by)
IT 123536-13-0
RL: BIOL (Biological study)
(**catalytic antibody** with lactone synthase activity inhibition by)
IT 111640-16-5P
RL: PREP (Preparation)
(preparation of, as substrate for **catalytic antibody** with lactone synthase activity)
IT 123440-96-0P
RL: PREP (Preparation)
(preparation of, as transition state analog for **catalytic antibody** production)
IT 18352-28-8P 123440-92-6P 123440-93-7P 123440-94-8P 123440-95-9P
RL: PREP (Preparation)
(preparation of, in transition state analog preparation for **catalytic antibody** production)
IT 1119-51-3, 5-Bromo-1-pentene
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in transition analog preparation for **catalytic antibody** production)
IT 3426-89-9, Phenylphosphorodichloridite 117746-42-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in transition state analog preparation for **catalytic antibody** production)

L42 ANSWER 17 OF 22 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1985:111098 HCAPLUS
DOCUMENT NUMBER: 102:111098
TITLE: Shared idiotypy between phosphorylcholine-specific antibody and acetylcholinesterase detectable by a monoclonal antibody
AUTHOR(S): Strickland, Faith M.; Hamilton, Susan L.; Blalock, Edwin; Cerny, Jan
CORPORATE SOURCE: Med. Branch, Univ. Texas, Galveston, TX, 77550, USA
SOURCE: Journal of Immunology (1985), 134(2), 1053-8
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Studies were undertaken to detect structural similarities between Igs and other proteins that bind to choline-containing **ligands**. Such proteins may share serol. detectable determinants that may not be predicted from the amino acid sequence alone. A monoclonal antibody was used that recognized an idiotope near the phosphorylcholine binding site of the IgA myeloma TEPC15. This monoclonal anti-TEPC15 idiotopic antibody (anti-Id) also bound the enzyme acetylcholinesterase (AChE) as well as the nicotinic acetylcholine **receptor** from Torpedo californica. The anti-Id **antibody** also decreased the AChE **catalytic** activity but did not affect the activity of an unrelated enzyme, horseradish peroxidase. These findings suggest that nonimmunoglobulin

mols. share antigenic determinants with Ig that are associated with binding to structurally related **ligands**, and immune regulation may inadvertently affect the function of nonimmune systems.
CC 15-3 (Immunochemistry)

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YOU HAVE REQUESTED DATA FROM 5 ANSWERS - CONTINUE? Y/(N):y

L42 ANSWER 18 OF 22 USPATFULL on STN

ACCESSION NUMBER:	2003:6968 USPATFULL			
TITLE:	GDNF receptor			
INVENTOR(S):	Klein, Robert D., South San Francisco, CA, United States Moore, Mark W., San Francisco, CA, United States Rosenthal, Arnon, Burlingham, CA, United States Ryan, Anne M., Millbrae, CA, United States			
PATENT ASSIGNEE(S):	Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6504007	B1	20030107	
	WO 9733912		19970918	<--
APPLICATION INFO.:	US 1997-860370		19970606	(8)
	WO 1997-US4363		19970313	
			19970606	PCT 371 date
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1996-618236, filed on 14 Mar 1996, now abandoned Continuation-in-part of Ser. No. US 1996-615902, filed on 14 Mar 1996, now abandoned			
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	GRANTED			
PRIMARY EXAMINER:	Kunz, Gary L.			
ASSISTANT EXAMINER:	Hayes, Robert C.			
LEGAL REPRESENTATIVE:	Knobbe, Martens, Olson & Bear, LLP			
NUMBER OF CLAIMS:	2			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	20 Drawing Figure(s); 14 Drawing Page(s)			
LINE COUNT:	4881			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB GDNFRα, GDNFRα extracellular domain (ECD), GDNFRα variants, chimeric GDNFRae (e.g., GDNFRα immunoadhesin), and antibodies which bind thereto (including agonist and neutralizing antibodies) are disclosed. Various uses for these molecules are described, including methods to **modulate** cell activity and survival by response to GDNFRα-ligands, for example GDNF, by providing GDNFRα to the cell. Also provided are methods for using GDNFRα, GDNF, or agonists thereof, separately or in complex, to treat kidney diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 6504007 B1 20030107
WO 9733912 19970918 <--
AB . . . which bind thereto (including agonist and neutralizing antibodies) are disclosed. Various uses for these molecules are described, including methods to **modulate** cell activity and survival by response to GDNFRα-ligands, for example GDNF, by providing GDNFRα to the cell. Also provided are. . .

SUMM . . . (preferably GDNF) responsiveness to cells. This responsiveness includes ligand-binding, Ret tyrosine phosphorylation and Ret-mediated downstream activity, which can result in **modulation** of cell activity such as survival or growth. The embodiments find use in vivo, in vitro or ex vivo. The. . .

SUMM Antibodies are provided that specifically bind to GDNFRα. Preferred antibodies are monoclonal antibodies that are **non-immunogenic** in a human and bind to an epitope in the extracellular domain of the receptor. Preferred antibodies bind the GDNFRα. . .

DETD "**Non-immunogenic** in a human" means that upon contacting the polypeptide of interest in a physiologically acceptable carrier and in a therapeutically. . .

DETD . . . hormones such as follicle stimulating hormone (FSH), thyroid stimulating hormone (TSH), and luteinizing hormone (LH); hepatic growth factor; fibroblast growth **factor**; prolactin; placental lactogen; **tumor necrosis factor**-. **alpha**. and -β; mullerian-inhibiting substance; mouse gonadotropin-associated peptide; inhibin; activin; vascular endothelial growth factor; integrin; thrombopoietin (TPO); neurotrophic factors or nerve. . .

DETD . . . the isolation, sequence, and tissue distribution of a novel GPI-linked protein and its gene, designated GDNFRα, which is shown to **modulate** cell response to GDNF. Ligand bound GDNFRα induces phosphorylation of the tyrosine kinase receptor Ret. These findings identify Ret and. . .

DETD . . . two of which (G1 m and 2) are located in the Fc region; and one of these sites GIml, is **non-immunogenic**. In contrast, there are 12 serologically-defined allotypes in IgG3, all of which are in the Fc region; only three of these sites (G3 m5, 11 and 21) have one allotype which is **nonimmunogenic**. Thus, the potential immunogenicity of a γ3 immunoadhesin is greater than that of a γ1 immunoadhesin.

DETD . . . interconnected networks called plexuses. Of these, the myenteric plexus, situated between the circular and longitudinal muscle layers, is the main **modulator** of gastrointestinal motility. It receives input from both the central nervous system (via vagal and sympathetic pathways) as well as. . .

DETD . . . bloating) are manifestations of increased motility in the gut and hyper-secretion of gastric acid. Activity of the GI tract is **modulated** neurally by the central nervous system (CNS) via parasympathetic and sympathetic innervation and by the peripherally located enteric nervous system. . .

DETD . . . when the patient is human. Human mature GDNF (WO 93/06116) is the preferred form of GDNF. The implants are preferably **non-immunogenic** and/or prevent immunogenic implanted cells from being recognized by the immune system. For CNS delivery, a preferred location for the. . .

DETD The GDNFRα (polypeptide or nucleic acid) can be used to increase GDNF-responsiveness (and thus increase cell survival and **modulate** Ret-mediated downstream pathways) of cells in vitro. Such cells must contain or be modified to contain cell surface Ret. Cultured. . .

DETD . . . invention, cells may be incubated for about 30 minutes in the presence of tagged GDNF. If the tag is an **antibody** molecule, it may be preferable to allow GDNF to bind to cells first and subsequently wash the cells to remove unbound ligand, followed by adding anti-GDNF **antibody** tag. In another embodiment of the invention, tagged GDNF on the surface of GDNF-responsive cells,

hereafter called target cells, may. . . of target cells may be detected using immunofluorescent techniques in which a molecule which reacts with the tag, preferably an **antibody**, directly or indirectly produces fluorescent light. The fluorescence may either be observed under a microscope or used to segregate tagged-GDNF-bearing. . . sorting techniques. The present invention also provides for methods for detecting other forms of tags, such as chromogenic tags and **catalytic** tags. An anti-GDNFR **antibody** can also be used as a probe. The detection methods for any particular tag will depend on the conditions necessary. . .

DETD . . . on GDNF and the discovery of the receptor and associated receptor system for GDNF, presented herein, provide the means for **modulating** and controlling cell activity and survival. This provides additional and specific methods of treatment available to the clinician.

L42 ANSWER 19 OF 22 USPATFULL on STN

ACCESSION NUMBER:	2001:82578 USPATFULL
TITLE:	IkB kinase, subunits thereof, and methods of using same
INVENTOR(S):	Karin, Michael, San Diego, CA, United States DiDonato, Joseph A., Westlake, OH, United States Rothwarf, David M., La Jolla, CA, United States Hayakawa, Makio, Tokyo, Japan Zandi, Ebrahim, Duarte, CA, United States
PATENT ASSIGNEE(S):	Regents of the University of California, Oaland, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6242253	B1	20010605	<--
APPLICATION INFO.:	US 1998-168629		19981008	(9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-61470P	19971009 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Prouty, Rebecca E.
ASSISTANT EXAMINER:	Monshipouri, Maryam
LEGAL REPRESENTATIVE:	Medlen & Carroll, LLP
NUMBER OF CLAIMS:	11
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	5 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT:	2524

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides an isolated nucleic acid molecules encoding IKB kinase (IKK) **catalytic** subunit polypeptides, which are associated with an IKK serine protein kinase that phosphorylates a protein (IKB) that inhibits the activity of the NF-KB transcription factor, vectors comprising such nucleic acid molecules and host cells containing such vectors. In addition, the invention provides nucleotide sequences that can bind to a nucleic acid molecule of the invention, such nucleotide sequences being useful as probes or as antisense molecules. The invention also provides isolated IKK **catalytic** subunits, which can phosphorylate an IKB protein, and peptide portions of such IKK subunit. In addition, the invention provides anti-IKK **antibodies**, which specifically bind to an IKK complex or an IKK **catalytic** subunit, and IKK-binding fragments of such **antibodies**. The invention further provides

methods of substantially purifying an IKK complex, methods of identifying an agent that can alter the association of an IKK complex or an IKK **catalytic** subunit with a second protein, and methods of identifying proteins that can interact with an IKK complex or an IKK **catalytic** subunit.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 6242253 B1 20010605 <--

AB The present invention provides an isolated nucleic acid molecules encoding IKB kinase (IKK) **catalytic** subunit polypeptides, which are associated with an IKK serine protein kinase that phosphorylates a protein (IKB) that inhibits the activity. . . . of the invention, such nucleotide sequences being useful as probes or as antisense molecules. The invention also provides isolated IKK **catalytic** subunits, which can phosphorylate an IKB protein, and peptide portions of such IKK subunit. In addition, the invention provides anti-IKK **antibodies**, which specifically bind to an IKK complex or an IKK **catalytic** subunit, and IKK-binding fragments of such **antibodies**. The invention further provides methods of substantially purifying an IKK complex, methods of identifying an agent that can alter the association of an IKK complex or an IKK **catalytic** subunit with a second protein, and methods of identifying proteins that can interact with an IKK complex or an IKK **catalytic** subunit.

SUMM . . . be, for example, a peptide, a polypeptide, a peptidomimetic or a small organic molecule. Such agents can be useful for **modulating** the level of phosphorylation of IKB in a cell, thereby **modulating** the activity of NF-KB in the cell and the expression of a gene regulated by NF-KB.

DETD . . . nucleotide and amino acid sequence homology. As disclosed herein, IKKα and IKKβ are related members of a family of IKK **catalytic** subunits (see FIG. 3). The 900 kDa IKB kinase complex can be isolated in a single step, for example, by immunoprecipitation using an **antibody** specific for an IKK subunit or by using metal ion chelation chromatography methods (see Example IV). A 300 kDa IKK. . .

DETD . . . human immunodeficiency virus-1 (HIV-1); immunoglobulin superfamily genes such as the MHC class 1 (H-2K) gene; cytokine genes such as the **tumor necrosis factor** . **alpha**. (**TNF**.**alpha**.), interleukin-1β (IL-1β), IL-2, IL-6 and the granulocyte-macrophage colony stimulating factor (GM-CSF) gene; chemokine genes such as RANTES and IL-8; and. . .

DETD . . . cycloheximide (Thanos and Maniatis, supra, 1995; Siebenlist et al., supra, 1994). Significantly, the expression of genes encoding agents such as **TNF**.**alpha**., IL-1, IL-6, interferon-β and various chemokines, which induce NF-KB activity, are, themselves, induced by NF-KB, resulting in amplification of their. . .

DETD . . . phosphorylated in the absence of MEKK1 (Lee et al., supra, 1997). However, a catalytically inactive MEKK1 mutant, which can block **TNF**.**alpha**. mediated activation of the jun kinase, does not block NF-KB activation (Liu et al., Cell 87:565-576 (1996)).

DETD . . . Moreover, an antisense PKR DNA molecule prevented NF-KB activation by double stranded RNA, but did not prevent NF-KB activation by **TNF**.**alpha**. (Maran et al., Science 265:789-792 (1995)). Casein kinase II (CKII) also can interact with and phosphorylate IKBα, although weakly as. . .

DETD As used herein, the term "isolated," when used in reference to an IKB

kinase complex or to an IKK **catalytic** subunit of the invention, means that the complex or the subunit is relatively free from contaminating lipids, proteins, nucleic acids. . . An isolated 900 kDa IKB kinase complex or 300 kDa complex can be isolated, for example, by immunoprecipitation using an **antibody** that binds to an IKK **catalytic** subunit (see Examples III and IV). In addition, an isolated IKK subunit can be obtained, for example, by expression of. . . cell by a method comprising affinity chromatography using ATP or IKB as ligands (Example I) or using an anti-IKK subunit **antibody**. An isolated IKK complex or IKK subunit comprises at least 30% of the material in a sample, generally about 50%. . .

DETD . . . can comprise an immunogenic amino acid sequence of the polypeptide and, therefore, can be useful for eliciting production of an **antibody** that can specifically bind the IKK subunit or to an IKK complex comprising the subunit, particularly to an epitope comprising. . . SEQ ID NO: 15, provided said epitope is not present in a CHUK protein. Accordingly, the invention also provides anti-IKK **antibodies**, which specifically bind to an epitope of an IKK complex, particularly an IKK **catalytic** subunit, and to IKK subunit binding fragments of such **antibodies**. In addition, the invention provides cell lines producing anti-IKK **antibodies** or IKK-binding fragments of such **antibodies**.

DETD As used herein, the term "**antibody**" is used in its broadest sense to include polyclonal and monoclonal **antibodies**, as well as antigen binding fragments of such **antibodies**. With regard to an anti-IKK **antibody** of the invention, the term "antigen" means an IKK **catalytic** subunit protein, polypeptide or peptide portion thereof, or an IKK complex comprising an IKK **catalytic** subunit protein, polypeptide or peptide portion thereof. Thus, it should be recognized that, while an anti-IKK **antibody** can bind to and, for example, immunoprecipitate an IKK complex, the **antibody** specifically binds an epitope comprising at least a portion of an IKK **catalytic** subunit. An **antibody** of the invention also can be used to immunoprecipitate an IKK subunit, free of the IKK complex.

DETD Anti-IKK **antibodies** can be raised using as an immunogen an isolated full length IKK **catalytic** subunit, which can be prepared from natural sources or produced recombinantly, or a peptide portion of an IKK subunit as defined herein, including synthetic peptides as described above. A **non-immunogenic** peptide portion of an IKK **catalytic** subunit can be made immunogenic by coupling the hapten to a carrier molecule such bovine serum albumin (BSA) or keyhole. . . sequences of IKKα polypeptides, as well as IKKβ polypeptides, likely are highly conserved among species, particularly among mammalian species. However, **antibodies** to highly conserved proteins have been raised successfully, for example, in chickens. Such a method can be used to obtain an **antibody** to an IKK subunit, if desired.

DETD A monoclonal anti-IKK **antibody** can be used to prepare anti-idiotypic **antibodies**, which present an epitope that mimics the epitope recognized by the monoclonal **antibody** used to prepare the anti-idiotypic **antibodies**. Where the epitope to which the monoclonal **antibody** includes, for example, a portion of the IKK **catalytic** subunit kinase domain, the anti-idiotypic **antibody** can act as a competitor of IKB and, therefore, can be useful for reducing the level of phosphorylation of IKB. . .

DETD . . . the invention provides a means to identify an agent that alters the association of an IKK complex or an IKK **catalytic** subunit with a second protein such as the regulatory subunits discussed above.

As used herein, the term "**modulate**" or "alter" when used in reference to the association of an IKK and a second protein, means that the affinity. . . of an agent. Agents that can alter the association of an IKK with a second protein can be useful for **modulating** the level of phosphorylation of IKB in a cell, which, in turn, **modulates** the activity of NF-KB in the cell and the expression of a gene regulated by NF-KB. Such an agent can be, for example, an anti-idiotypic **antibody** as described above, which can inhibit the association of an IKK and IKB. A peptide portion of IKBα comprising amino. . .

DETD . . . inhibitors or on ATP or adenosine can be screened using an assay of the invention to obtain agents that desirably **modulate** the activity of an IKK complex or an IKK subunit.

DETD . . . screening assay of the invention is particularly useful to identify, from among a diverse population of molecules, those agents that **modulate** the association of an IKK complex or an IKK catalytic subunit and another protein (referred to herein as a "second. . .

DETD . . . molecules, a screening assay of the invention provides a simple means for identifying those agents in the library that can **modulate** the association of an IKK and a second protein or can alter the activity of an IKK. In particular, a. . . automated, which allows for high through-put screening of randomly designed libraries of agents to identify those particular agents that can **modulate** the ability of an IKK and a second protein to associate or that alter the activity of the IKK.

DETD . . . the ability to specifically associate with an appropriate second protein such as an IKB protein. For example, when an IKK **catalytic** subunit is used in a screening assay, the solid substrate can contain a covalently attached anti-IKK **antibody**, provided that the **antibody** binds the IKK subunit without interfering with the ability of the IKK subunit to associate with the second protein. Where. . .

DETD . . . can be determined and compared to the amount of binding in the absence of the agent so that agents that **modulate** the association can be identified.

DETD . . . such as an IKB or for altering the activity of an IKK. Such agents can be useful, for example, for **modulating** the activity of NF-KB in a cell and, therefore, can be useful as medicaments for the treatment of a pathology. . .

DETD The invention also provides a method of obtaining an isolated IKK complex or an IKK **catalytic** subunit. For example, a 300 kDa or a 900 kDa IKK complex, comprising an IKKα subunit can be isolated from a sample by immunoprecipitation using an anti-IKKα **antibody** or by tagging the IKKα and using an **antibody** specific for the tag (see Examples III and IV). In addition, an IKK **catalytic** subunit can be isolated from a sample by 1) incubating the sample containing the IKK subunit with ATP, which is. . . suitable for binding of the IKK subunit to the IKB; and 4) obtaining from the immobilized IKB an isolated IKK **catalytic** subunit. Such a method of isolating an IKK subunit is exemplified herein by the use of ATP affinity chromatography and. . .

DETD The skilled artisan will recognize that a ligand such as ATP or an IKB or an anti-IKK **antibody** also can be immobilized on various other matrices, including, for example, on magnetic beads, which provide a rapid and simple. . . IKK from the remainder of the sample. Methods for immobilizing a ligand such as ATP or an IKB or an **antibody** are well known in the art (Haystead et al., Eur. J. Biochem. 214:459-467 (1993), which is incorporated herein by reference;. . . and prepared

as a lysate; or can be a bacterial, insect, yeast or mammalian cell lysate, in which an IKK **catalytic** subunit is expressed from a recombinant nucleic acid molecule. As disclosed herein, a recombinantly expressed IKKα or IKKβ such as. . .

DETD . . . useful for the manipulation of protein--protein interaction and, therefore, also is useful in a screening assay to identify agents that **modulate** the specific interaction.

DETD . . . or inhibiting expression of the IKK subunit or by reducing or inhibiting its responsiveness to an inducing agent such as **TNF** .**alpha**., Il-1 or phorbol ester (see Example II). Accordingly, the invention also provides methods of treating an individual suffering from a pathology characterized by aberrant NF-KB activity by administering to the individual an agent that **modulates** the catalytic activity of an IKK or that alters the association of an IKK subunit and a second protein such. . .

DETD In order to activate the IKK, cells were stimulated with **TNF**. **alpha**. prior to purification. **TNF**.**alpha**. was either recombinant **TNF**.**alpha**., which was purchased from R&D Systems and used at 20 ng/ml, or HIS6-tagged **TNF**. **alpha**., which was expressed and partially purified from E. coli and used at 5 μg/ml. **TNF**.**alpha**.-induced HeLa S3 cell killing activity assays were performed in the presence of cycloheximide and indicated that the partially purified HIS6-tagged **TNF**.**alpha**. had approximately one-tenth the activity of the commercial **TNF**.**alpha**..

DETD . . . was approximately 5+10.sup.5 cells/ml at the time of collection. Cells were concentrated 10-fold by centrifugation. stimulated for 5 min with **TNF**.**alpha**. at 37° C., then diluted with 2.5 volumes of ice cold phosphate buffered saline (PBS) containing 50 mM NaF and. . .

DETD . . . liquid nitrogen and stored at -80° C. Small aliquots of S100 material, prepared from either unstimulated HeLa cells or from **TNF**.**alpha**. stimulated cells, were purified in a single passage over a SUPEROSE 6 gel filtration column (1.0+30 cm; Pharmacia; Uppsalla Sweden). . . collected and kinase assays were performed on an aliquot of each fraction. The high molecular weight material (fractions 16-20) contained **TNF**.**alpha** .-inducible IKK activity, which is specific for the WT substrate.

DETD . . . were collected and the kinase assay was performed on those fractions that eluted during the gradient. Fractions corresponding to the **TNF**.**alpha**.-inducible IKK activity (fractions 30-42; i.e., 20-32 of the gradient portion) were pooled. The pooled material contained 40 mg of protein.

DETD Cytoplasmic extract was prepared using HeLa S3 cells. The cells were stimulated with **TNF**.**alpha**. for 5 min, then harvested in lysis buffer containing 0.1% NP-40 and 0.15 M NaCl. Reactivation was performed at 30°. . .

DETD . . . growth medium was replaced with DMEM containing 0.1% FBS. Cells either were left untreated, or were treated with 20 ng/ml **TNF**. **alpha**., 20 ng/ml IL-1α, or 100 ng/ml TPA (phorbol ester) for 3.5 hr. Cells were harvested by scraping and washed once. . .

DETD . . . is known to induce expression for the IL-8 promotor. Thus, as expected, treatment of the vector transfected control cells with **TNF**.**alpha**., IL-1.**alpha**. or TPA resulted in a 3- to 5-fold increase in normalized luciferase activity. In comparison, in cells transfected with the cDNA encoding IKK.**alpha**., treatment with **TNF**.**alpha**., IL-1.**alpha**. or TPA potentiated induction of luciferase activity 5- to 6-fold above the level of induction observed in the vector transfected. . .

DETD . . . with the vector expressing the antisense IKKα nucleic acid molecule, transcription of the luciferase reporter gene induced by IL-1 or **TNF.alpha**. was at the limit of detection, indicating transcription was almost completely inhibited due to expression of the antisense IKKα. This. . .

DETD . . . IKKα. Expression of increasing amounts of HA-IKKβ resulted in higher basal levels of IKK activity and increasing amounts of coprecipitated IKK.**alpha**.. The level of **TNF** stimulated IKK activity increased only marginally in response to IKKβ overexpression and TNF had no effect on the association of. . .

DETD . . . stimulated IKK activity that, after TNF stimulation, was 2- to 3-fold lower than the activity of IKK formed by wt HA-IKK.**alpha** . isolated from **TNF**-stimulated cells. Similarly, expression and immunoprecipitation of HA-IKKβ resulted in formation of a cytokine responsive IKK activity that, after TNF stimulation,. . .

DETD . . . IKK activity was detected in cells expressing HF-IKKα and IKK activity increased several fold when the cells were treated with **TNF.alpha**.. This result indicates that the HF-IKKα expression in 293 cells is associated with IKK activity in the cells and that such IKK activity is inducible in response to **TNF.alpha**..

DETD . . . cell line that expresses HF-IKKα was selected and expanded to approximately 4+10.sup.8 cells. The cells were treated with 10 ng/ml **TNF.alpha**. for 5 min, then harvested in ice cold PBS by centrifugation at 2500+g. The cell pellet was washed with ice. . .

L42 ANSWER 20 OF 22 USPATFULL on STN

ACCESSION NUMBER:	2001:36798 USPATFULL			
TITLE:	Chitinase chitin-binding fragments			
INVENTOR(S):	Gray, Patrick W., Seattle, WA, United States Tjoelker, Larry W., Kirkland, WA, United States			
PATENT ASSIGNEE(S):	ICOS Corporation, Bothell, WA, United States (U.S. corporation)			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6200951	B1	20010313	<--
APPLICATION INFO.:	US 1998-39198		19980312 (9)	
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Prouty, Rebecca E.			
LEGAL REPRESENTATIVE:	Marshall, O'Toole, Gerstein, Murray, & Borun			
NUMBER OF CLAIMS:	10			
EXEMPLARY CLAIM:	1			
LINE COUNT:	1721			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides chitin-binding fragments of human chitinase, fragment analogs, purified and isolated polynucleotide sequences encoding such fragments and analogs, and materials and methods for the recombinant production of human chitinase fragment products which are expected to be useful as in products for detecting chitin, binding chitin, and treating fungal infections or for development of products useful for treating the same.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

PI US 6200951 B1 20010313 <--

SUMM . . . for proteins or other molecules (e.g., small molecules) that

specifically bind to the chitin-binding domain of human chitinase or that **modulate** binding of human chitinase to chitin or to human extracellular matrix proteins such as hyaluronic acid. Proteins or other molecules. . . cells expressing such products. Proteins or other molecules that bind to the chitin-binding domain of chitinase may be used to **modulate** its activity. Binding proteins specific for chitinase are contemplated by the invention and include antibody substances (e.g., monoclonal and polyclonal. . .

SUMM . . . express a variant chitinase enzyme. Such animals are useful as models for studying the in vivo activity of chitinase or **modulators** of chitinase. Polynucleotides of the invention when suitably labelled are useful in hybridization assays to detect the capacity of cells. . .

SUMM . . . purpose is more advantageous than using chitin-binding domains of chitinases of other species because human polypeptides are expected to be **non-immunogenic** in humans.

SUMM . . . known to be closely associated with rheumatoid arthritis lesions [Feldman et al., Cell, 85:307-310 (1996)], and macrophage products such as **TNF**-.**alpha**. are implicated in disease progression. A protein with homology to human chitinase, C-gp39, has been detected in the synovium and. . . before and after chitinase treatment; a decrease of viscosity associated with chitinase would be consistent with an endogenous chitinase substrate. **Modulation** of chitinase activity could thereby **modulate** the progression of joint destruction in rheumatoid arthritis.

SUMM . . . describes production of human chitinase fragments having chitin-binding activity and analogs thereof. Example 8 provides a protocol for generating monoclonal **antibodies** that are specifically immunoreactive with human chitinase. Example 9 describes an assay for the measurement of chitinase **catalytic** activity. Example 10 addresses determination of the anti-fungal activity of test drugs in vitro. Example 11 addresses determination of the. . .

L42 ANSWER 21 OF 22 USPATFULL on STN

ACCESSION NUMBER:	2001:33321 USPATFULL
TITLE:	Azulenyl nitrone spin trapping agents, methods of making and using same
INVENTOR(S):	Becker, David Alan, Ft. Lauderdale, FL, United States
PATENT ASSIGNEE(S):	Florida International University, Miami, FL, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6197825	B1	20010306	<--
APPLICATION INFO.:	US 1998-85170		19980528 (9)	
RELATED APPLN. INFO.:	Division of Ser. No. US 1997-944042, filed on 9 Apr 1997 Continuation of Ser. No. WO 1996-US18570, filed on 15 Nov 1996			

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-6949P	19961115 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	O'Sullivan, Peter
LEGAL REPRESENTATIVE:	Villacorta, Gilberto M.
NUMBER OF CLAIMS:	5
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	2 Drawing Figure(s); 1 Drawing Page(s)

LINE COUNT: 1985
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to chromotropic nitrone spin trapping agents, methods of making these agents, compositions comprising same, and methods of their use. In particular, azulenyl nitrones of the present invention are effective agents for trapping free radical species and find use as efficient antioxidants in physicochemical and biological systems. Accordingly, the invention also relates to spin adducts formed from the combination of azulenyl nitrones with free radicals. The compounds of the present invention are readily prepared from available starting materials and find further use in assays and in a number of diagnostic, prophylactic and therapeutic applications, including but not limited to the alleviation, **modulation** and inhibition of the negative effects of carbon-centered or oxygen-centered radical species and other products of oxidation. Moreover, the combination adducts may be calorimetrically detected and, optionally, isolated and characterized to obtain valuable information (e.g., structural and the like) about the original reactive free radical species.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 6197825 B1 20010306 <--
AB . . . use in assays and in a number of diagnostic, prophylactic and therapeutic applications, including but not limited to the alleviation, **modulation** and inhibition of the negative effects of carbon-centered or oxygen-centered radical species and other products of oxidation. Moreover, the combination. . .
SUMM Low molecular weight nitroxides are **non-immunogenic**. Moreover, they are typically cell permeable and can exist as a non-toxic, stable free radical capable of partitioning among various. . .
DETD . . . synthesis of these nitrones, one can envision making a wide range of easily prepared derivatives whose physical properties can be **modulated** by judicious choice of a nucleophile (alcohol, amine, etc.) to employ in acylation reactions with 2. Lipophilic or hydrophilic side. . .
DETD . . . 1 (Nu=OEt) or the sodium salt of Compound #4 (Nu=OH), is meant a sufficient amount of the compound to alleviate, **modulate**, or inhibit the negative or, otherwise, ill effects of free radical species and/or associated medical disorders at a reasonable benefit/risk. . .
DETD Hence, the azulenyl nitrone compounds of the present invention can be used in a method of treating, alleviating, **modulating**, or inhibiting the effects in the heart or brain of ischemia or reperfusion injury, acute respiratory distress syndrome (ARDS), sepsis,. . .
DETD . . . Procedure A (substitute an antisense oligonucleotide, like poly(dG).sub.10, for EtOH), then B, then C.
Compound #13 Procedure A (substitute a monoclonal **antibody** [NB: any monoclonal Ab listed in ATCC Catalog, for instance] for EtOH), then B, then C.
Compound #14 Procedure A (substitute. . . rt, then B, then C.
Compound #28 Same as Compound #27 except hydrolyze with NaOH before subjecting to Procedure B.
Compound #29 **Catalytic** hydrogenation of lactaroviolin, then nitration with HNO.sub.3 /H.sub.2 SO.sub.4 at 0° C. in AcOH, then Procedure C.
Compound #30 Wittig reaction. . . Procedure C.
Compound #32 Same as for Compound #1 substituting PbNHOH .multidot. HCl for tert-butylNHOH .multidot. HCl in Procedure C.
Compound #33 **Catalytic** hydrogenation of lactaroviolin, then Procedure C.

Compound #34 Starting with 1,3-Azulenedicarboxaldehyde [Ref: Hafner, K. and Bernhard, C., Annalen (1959) 625:108] obtain

. . .

DETD . . . is administered to 16 male Sprague-Dawley Rats to induce organ dysfunction and the secretion of a variety of cytokines, including **tumor necrosis factor-alpha** (**TNF-alpha**), interleukin-1 **alpha** (IL-1 alpha) and interleukin-1 beta (IL-1 beta). Thirty to forty-five minutes prior to LPS administration, half of the rats are. . .

DETD . . . edema. This nitrone also exhibits some inhibition of both thrombocytopenia and leukopenia. Moreover, marked decreases in serum levels of LPS-stimulated **TNF-alpha** IL-1 **alpha** and IL-1 beta are observed.

L42 ANSWER 22 OF 22 USPATFULL on STN
ACCESSION NUMBER: 2000:18243 USPATFULL
TITLE: Neurturin receptor
INVENTOR(S): Klein, Robert D., Palo Alto, CA, United States
Rosenthal, Arnon, Burlingame, CA, United States
Hynes, Mary A., San Mateo, CA, United States
PATENT ASSIGNEE(S): Genentech, Inc., United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6025157		20000215	<--
APPLICATION INFO.:	US 1997-957063		19971024	(8)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-38839P	19970218 (60)
	US 1997-49818P	19970609 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Campell, Bruce R.
ASSISTANT EXAMINER: Chen, Shin-Lin
LEGAL REPRESENTATIVE: Knobbe, Martens Olson & Bear, LLP
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 22 Drawing Figure(s); 23 Drawing Page(s)
LINE COUNT: 5116
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB NTNRα, NTNRα extracellular domain (ECD), NTNRα variants, chimeric NTNRα (e.g., NTNRα immunoadhesin), and antibodies which bind thereto (including agonist and neutralizing antibodies) are disclosed. Various uses for these molecules are described, including methods to **modulate** cell activity and survival by response to NTNRα-ligands, for example NTN, by providing NTNRα to the cell.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 6025157 20000215 <--
AB . . . which bind thereto (including agonist and neutralizing antibodies) are disclosed. Various uses for these molecules are described, including methods to **modulate** cell activity and survival by response to NTNRα-ligands, for example NTN, by providing NTNRα to the cell.
SUMM . . . (preferably NTN) responsiveness to cells. This responsiveness includes ligand-binding, Ret tyrosine phosphorylation and Ret-mediated downstream activity, which can result in **modulation** of cell

activity such as survival or growth. The embodiments find use in vivo, in vitro or ex vivo. Soluble. . .

SUMM Antibodies are provided that specifically bind to NTNRα. Preferred antibodies are monoclonal antibodies that are **non-immunogenic** in a human and bind to an epitope in the extracellular domain of the receptor. Preferred antibodies bind the NTNRα. . .

DETD "**Non-immunogenic** in a human" means that upon contacting the polypeptide of interest in a physiologically acceptable carrier and in a therapeutically. . .

DETD . . . hormones such as follicle stimulating hormone (FSH), thyroid stimulating hormone (TSH), and luteinizing hormone (LH); hepatic growth factor; fibroblast growth **factor**; prolactin; placental lactogen; **tumor necrosis factor-**. **alpha**. and -β; mullerian-inhibiting substance; mouse gonadotropin-associated peptide; inhibin; activin; vascular endothelial growth factor; integrin; thrombopoictin (TPO); neurotrophic factors or nerve. . .

DETD . . . is the isolation, sequence, and tissue distribution of a GPI-linked protein and its gene, designated NTNRα, which is shown to **modulate** response to NTN but not GDNF. It is shown herein that it is structurally related to GDNFRα. Using recombinant proteins. . .

DETD . . . sites, two of which (G1m and 2) are located in the Fc region; and one of these sites G1m1, is **non-immunogenic**. In contrast, there are 12 serologically-defined allotypes in IgG3, all of which are in the Fc region; only three of these sites (G3m5, 11 and 21) have one allotype which is **nonimmunogenic**. Thus, the potential immunogenicity of a γ3 immunoadhesin is greater than that of a γ1 immunoadhesin.

DETD . . . interconnected networks called plexuses. Of these, the myenteric plexus, situated between the circular and longitudinal muscle layers, is the main **modulator** of gastrointestinal motility. It receives input from both the central nervous system (via vagal and sympathetic pathways) as well as. . .

DETD . . . bloating) are manifestations of increased motility in the gut and hyper-secretion of gastric acid. Activity of the GI tract is **modulated** neurally by the central nervous system (CNS) via parasympathetic and sympathetic innervation and by the peripherally located enteric nervous system. . .

DETD . . . secrete NTNRα. Preferably, the secreted NTNRα being soluble, human mature NTNRα when the patient is human. The implants are preferably **non-immunogenic** and/or prevent immunugenic implanted cells from being recognized by the immune system. For CNS delivery, a preferred location for the. . .

DETD The NTNRα (polypeptide or nucleic acid) can be used to increase NTN-responsiveness (and thus increase cell survival and **modulate** Ret-mediated downstream pathways) of cells in vitro. Such cells must contain or be modified to contain cell surface Ret. Cultured. . .

DETD . . . invention, cells may be incubated for about 30 minutes in the presence of tagged NTN. If the tag is an **antibody** molecule, it may be preferable to allow NTN to bind to cells first and subsequently wash cells to remove unbound ligand and then add anti-NTN **antibody** tag. In another embodiment of the invention, tagged NTN on the surface of NTN-responsive cells, hereafter called target cells, may. . . of target cells may be detected using immunofluorescent techniques in which a molecule which reacts with the tag, preferably an **antibody**, directly or indirectly produces fluorescent light. The fluorescence may either be observed under a microscope or used to

segregate tagged-NTN-bearing. . . sorting techniques. The present invention also provides for methods for detecting other forms of tags, such as chromogenic tags and **catalytic** tags. An anti-NTNRα **antibody** can also be used as a probe. The detection methods for any particular tag will depend on the conditions necessary. . .

DETD . . . highlights the diverse strategies which are used to transmit extracellular signals in the vertebrate nervous system, and provides means for **modulating** and controlling cell activity and survival that expand the treatment modalities available to the clinician.